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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/558,276	11/18/2005	Thomas Wisniewski	05986/100M536-US1	3691

7278 7590 03/31/2009

DARBY & DARBY P.C.
P.O. BOX 770
Church Street Station
New York, NY 10008-0770

EXAMINER	
BOESEN, AGNIESZKA	
ART UNIT	PAPER NUMBER
1648	

MAIL DATE	DELIVERY MODE
03/31/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/558,276	WISNIEWSKI ET AL.	
	Examiner	Art Unit	
	AGNIESZKA BOESEN	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 January 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,4,9-13,15-23,28-31,33-37,40,45 and 46* is/are pending in the application.

4a) Of the above claim(s) *11-13,15-19,29-31,33-37 and 40* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,4,9,10,20,22,23,28,45 and 46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on January 15, 2009 has been entered.

Claims 2, 5-8, 14, 21, 24-27, 32, 38, 39, 41-44 and 47-50 have been canceled. Rejections of canceled claims are moot. Claims 11-13, 15-19, 29-31, 33-37 and 40 are withdrawn.

Claims 1, 3, 9, 10, 20, 22, 23, 28, 45 and 46 are under examination in this Office Action.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Rejection of claim 28 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement **is maintained.** It is apparent that the *Salmonella* spp strains, *Salmonella typhimurium* LVR01, LVR03, and SL3261, *Salmonella enteritidis* LVR02, and *Salmonella typhi* CVD915 are required to practice the claimed invention because they are a necessary limitation for the success of the invention as stated in the claims. As a required element it must be known and readily available to the public or obtainable by a repeatable method set forth in the specification, or otherwise readily available to the public. If it is not so

obtainable or available, the enablement requirements of 35 U.S.C. § 112, first paragraph, may be satisfied by a deposit of the *Salmonella typhimurium* LVR01, LVR03, and SL3261, *Salmonella enteritidis* LVR02, and *Salmonella typhi* CVD915 strains. See 37 CFR 1.802.

Applicants request that rejection be held in abeyance until one or more claims are found to be allowable.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Rejection of Claim 3 35 U.S.C. 103(a) as being unpatentable over Bachmann et al. (Patent Application Publication No.: 2003/0219459 A1) in view of Gizurarson et al. (US Patent 6,514,503 B1) **is withdrawn** in view of Applicant's amendment and arguments.

Rejection of Claims 1 and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bachmann et al. (Patent Application Publication No.: 2003/0219459 A1) in view of Gizurarson et al. (US Patent 6,514,503 B1) **is maintained.**

Rejection of Claim 4 35 U.S.C. 103(a) as being unpatentable over Bachmann et al. (Patent Application Publication No.: 2003/0219459 A1) and Gizurarson et al. (US Patent 6,514,503 B1) as applied to claim 1 and further in view of Benkirane et al. (Journal of Biological Chemistry, 1993, Vol. 268, p. 26279-26285, in IDS of 11/18/2005) **is maintained.**

Rejection of Claims 9 and 10 35 U.S.C. 103(a) as being unpatentable over Bachmann et al. (Application Publication No.: 2003/0219459 A1) and Gizurarson et al. (US Patent 6,514,503 B1)as applied to claim 1 and further in view of Clemens et al. (US Patent 6,440,423 B1) and Kleanthous et al. (US Patent 6,585,975 B1) **is maintained.**

Rejection of claim 45 under 35 U.S.C. 103(a) as being unpatentable over Bachmann et al. (Patent Application Publication No.: 2003/0219459 A1), Gizurarson et al. (US Patent 6,514,503 B1) and Lu et al. (US Patent 5,733,760) and further in view of Chabalgoity et al. (Vaccine, 2001, Vol. 19, p. 460-469, in IDS of 11/18/2005) **is withdrawn** in view of Applicant's amendment and arguments.

Rejection of Claims 20, 22 and 28 under 35 U.S.C. 103(a) as being unpatentable over Bachmann et al. (Patent Application Publication No.: 2003/0219459 A1), Gizurarson et al. (US Patent 6,514,503 B1) and Lu et al. (US Patent 5,733,760) and further in view of Chabalgoity et al. (Vaccine, 2001, Vol. 19, p. 460-469, in IDS of 11/18/2005) **is maintained.**

Rejection of Claims 23 and 46 under 35 U.S.C. 103(a) as being unpatentable over Bachmann et al. (Patent Application Publication No.: 2003/0219459 A1), Gizurarson et al. (US Patent 6,514,503 B1) and Lu et al. (US Patent 5,733,760) as applied to claims 22 and further in view of Benkirane et al. (Journal of Biological Chemistry, 1993, Vol. 268, p. 26279-26285) **is maintained.**

Response to Applicant's arguments

Applicant's arguments have been fully considered but fail to persuade. Applicant argues that Bachman teaches away from the use of isolated proteins because Bachman expressly teaches that isolated proteins including isolated prion proteins are inefficient for eliciting an immune

response. Applicant argues that Bachman rather teaches virus like particles bound to prion proteins.

In response to Applicant's arguments Examiner notes that the present claims are product claims and not method claims. Bachmans prion protein comprised in the VLP anticipates the presently claimed composition comprising an isolated prion protein. It is also noted that, contrary to Applicant's assertions Bachman's prion protein comprised in the VLP is an isolated prion protein, because the prion protein must first be isolated or synthetically made in order to be incorporated into a VLP.

Applicant argues that Bachman fails to teach or suggest compositions comprising aluminium hydroxide for mucosal delivery and that Bachman only teaches using aluminum hydroxide for parenteral administration. In response to Applicant's arguments the Examiner noted that because Bachman discloses a composition comprising prion protein and aluminum hydroxide Bachman teaches the claimed compositions. It is the position of the Office that the mucosal versus perenteral administration is viewed as intended use and does not confer further substance to the claimed composition.

Applicant argues that Gizarurson does not remedy the deficiencies in the Bachman's reference, because Gizarurson does not teach compositions comprising prion proteins. In response the Examiner notes that Gizaruson provides a motivation to use mucosal administration of pathogenic antigens, because Gizurarson teaches that his compositions formulated for mucosal administration provide enhanced adhesion of the antigen to the mucosal membrane and enhance absorption of the antigen through the mucus membrane, and that the mucosal administration provides the ability to elicit both a systemic (e.g., antibodies of the IgG isotype) and a local (e.g.,

secretory antibodies of the IgA isotype) immune response in the recipients of the composition without causing unacceptable irritation of the epithelial membrane (see column 2, lines 48-65), as discussed on the record. Applicant cites a reference by Czerkinsky and argues that administration of self antigen such as prion protein would lead to immune tolerance to that antigen and that Czerkinsky teaches that mucosal tolerance is considered a major adaptive immune defense mechanism to avoid harmful immune responses against dietary and airborne antigens. In response the Examiner notes that the pathogenic form of prion protein is not considered self antigen and therefore it would have been expected that when administered mucosally it would induce immune responses against the prion protein as suggested by Gizarurson. It has been well known in the art that mucosal administration of antigens together with adjuvants results in generation of immune response as taught by Gizarurson.

Applicant argues that Clemens and Kleanthous fail to remedy the deficiencies of Bachman and Gizarurson, because Kleanthous only teaches eliciting Th1 response through parenteral administration. Applicants argue that the tolerance to mucosal antigens cannot be overcome by mucosal administration as taught by Czerkinsky. In response, the Examiner notes that the pathogenic prion protein is not considered in the art as the self antigen. Even if the pathogenic prion was a self antigen, it is well known in the art that induce immune response to self antigens by active immunization, for example mice immunized with their own DNA are known to generate anti-nuclear antibodies. As discussed above Gizurarson expressly teaches that his compositions formulated for mucosal administration provide enhanced adhesion of the antigen to the mucosal membrane and enhance absorption of the antigen through the mucus membrane, and that the mucosal administration provides the ability to elicit both a systemic (e.g.,

antibodies of the IgG isotype) and a local (e.g., secretory antibodies of the IgA isotype) immune response in the recipients of the composition. Thus administering Kleanthous cholera toxin subunit B in the composition of Bachman and Gizarurson would have been obvious to the skilled artisan at the time of the present invention.

Applicant argues that Lu and Chabalgoity fail to remedy the deficiencies in Bachman and Gizarusrson, because they are silent about the delivery of self-antigen such as prion protein. In response the Examiner noted that the immunization with prion protein is taught by Bachman, as discussed above. Lu and Chabalgoity are cited because they teach effectiveness of Samonella vectors in induction of mucosal immune responses.

Applicant argues that Benkirane fails to remedy the deficiencies of Bachman and Gizarusrson. In response it is noted that Benkirane is cited because Benkirane teaches the use of D-amino acids.

Thus because Bachman and Gizarusrson teach the claimed invention and because Clemens, Kleanthous, Lu, Chabalgoity and Benkirane remedy the deficiencies of Bachman and Gizarusrson as discussed above and on the record, the rejections are maintained.

New rejections

Claim 3 is rejected under 35 U.S.C. 103(a) as being unpatentable over Bachmann et al. (Patent Application Publication No.: 2003/0219459 A1) in view of Gizurarson et al. (US Patent 6,514,503 B1) and further in view of Peretz et al. (Nature 2001, Vol. 412, p. 739-743) and Kaneko et al. (JMB, 2000, Vol. 295, p. 997-1007).

Bachman et al. and Gizurarson et al. teach a composition comprising a mammalian prion protein that is suitable for mucosal administration, as discussed above.

While Bachman teaches presently claimed SEQ ID NO: 4, Bachman does not teach specifically using residues 93-156 of SEQ ID NO: 4.

Peretz teaches that the region spanning amino acids 132-156 of an isolated prion protein is a critical determinant for inhibition of prion propagation by antibodies binding those particular amino acids (see page 741, right paragraph). Kaneko teaches that residues 90-144 of human prion protein are important for initiating prion disease (see Results and Table 1).

It would have been prima facie obvious and one would have been motivated to provide Bachman's prion composition consisting of residues 93-156 of the prion protein, because Peretz and Kaneko teach that residues 132-156 and 90-144 are critical for generation of neutralizing antibodies and are important for initiating prion disease. Thus since the prior art teaches that prion protein amino acid residues 90-156 contain the antibody epitopes and are critical for infection, the skilled artisan would have been motivated to provide presently claimed prion protein residues 93-156 for immunization purposes. Absent any unexpected results, it would have been obvious to use prion protein amino acid residues 93-156 for immunization purposes.

One would have had a reasonable expectation of success to provide prion composition for mucosal administration because the guidance for providing such compositions is available in the art.

Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Claim 45 is rejected under 35 U.S.C. 103(a) as being unpatentable over Bachmann et al. (Patent Application Publication No.: 2003/0219459 A1), Gizurarson et al. (US Patent 6,514,503 B1) and Lu et al. (US Patent 5,733,760) and Chabalgoity et al. (Vaccine, 2001, Vol. 19, p. 460-469, in IDS of 11/18/2005) further in view of Peretz et al. (Nature 2001, Vol. 412, p. 739-743) and Kaneko et al. (JMB, 2000, Vol. 295, p. 997-1007).

Bachman, Gizurarson, Lu and Chabalgoity teach a composition comprising mammalian prion protein that is suitable for mucosal administration, as discussed above.

While Bachman teaches presently claimed SEQ ID NO: 4, Bachman does not teach specifically using residues 123-225 of SEQ ID NO: 4.

Peretz teaches that the region spanning amino acids 132-156 of an isolated prion protein is a critical determinant for inhibition of prion propagation by antibodies binding those particular amino acids (see page 741, right paragraph). Kaneko teaches that residues 90-144 of human prion protein are important for initiating prion disease.

It would have been *prima facie* obvious and one would have been motivated to provide Bachman's prion composition consisting of residues 123-225 of the prion protein, because Peretz and Kaneko teach that residues 132-156 and 90-144 are critical for generation of neutralizing antibodies and are important for initiating prion disease and the claimed residues 123-225 overlap with Peretz and Kaneko epitope containing prion residues. Absent any unexpected results, it would have been obvious to use prion protein amino acid residues 123-225 for immunization purposes.

One would have had a reasonable expectation of success to provide prion composition for mucosal administration because the guidance for providing such compositions is available in the art.

Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to AGNIESZKA BOESEN whose telephone number is (571)272-8035. The examiner can normally be reached on Monday through Friday from 9:00 AM to 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Agnieszka Boesen/
Examiner, Art Unit 1648